FILE 'REGISTRY' ENTERED AT 15:04:59 ON 12 APR 2004

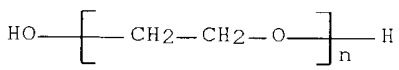
=> S PEG
           230 PEG
             2 PEGS
L1   232 PEG
                 (PEG OR PEGS)

=> S PEG/CN
L2   1 PEG/CN

=> D

L2   ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN   25322-68-3 REGISTRY
CN   Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy- (9CI) (CA INDEX
     NAME)
OTHER NAMES:
CN   α,ω-Hydroxypoly(ethylene oxide)
CN   α-Hydro-ω-hydroxypoly(oxy-1,2-ethanediyl)
CN   α-Hydro-ω-hydroxypoly(oxyethylene)
CN   1,2-Ethanediol, homopolymer
CN   1660O
CN   1660S
CN   400DAB8
CN   Alkox
CN   Alkox E 100
CN   Alkox E 130
CN   Alkox E 160
CN   Alkox E 240
CN   Alkox E 30
CN   Alkox E 45
CN   Alkox E 60
CN   Alkox E 75
CN   Alkox R 1000
CN   Alkox R 15
CN   Alkox R 150
CN   Alkox R 400
CN   Alkox SR
CN   Antarox E 4000
CN   Aquacide III
CN   Aquaffin
CN   Badimol
CN   BDH 301
CN   Bradsyn PEG
CN   Breox 2000
CN   Breox 20M
CN   Breox 4000
CN   Breox 550
CN   Breox PEG 300
CN   CAFO 154
CN   Carbowax
CN   Carbowax 100
CN   Carbowax 1000
CN   Carbowax 1350
CN   Carbowax 14000
CN   Carbowax 1450
CN   Carbowax 1500
CN   Carbowax 1540

CN Carbowax 20
CN Carbowax 200
CN Carbowax 20000
CN Carbowax 25000
CN Carbowax 300
CN Carbowax 3350
CN Carbowax 400
CN Carbowax 4000
CN Carbowax 4500
CN **PEG**
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
AR 9002-90-8
DR 615575-04-7, 12676-74-3, 12770-93-3, 9081-95-2, 9085-02-3, 9085-03-4, 54510-95-1, 125223-68-9, 54847-64-2, 59763-40-5, 64441-68-5, 64640-28-4, 133573-31-6, 25104-58-9, 25609-81-8, 134919-43-0, 101677-86-5, 99264-61-6, 106186-24-7, 112895-21-3, 114323-93-2, 50809-04-6, 50809-59-1, 119219-06-6, 60894-12-4, 61840-14-0, 37361-15-2, 112384-37-9, 70926-57-7, 75285-02-8, 75285-03-9, 77986-38-0, 150872-82-5, 154394-38-4, 79964-26-4, 80341-53-3, 85399-22-0, 85945-29-5, 90597-70-9, 88077-80-9, 88747-22-2, 34802-42-1, 107502-63-6, 107529-96-4, 116549-90-7, 156948-19-5, 169046-53-1, 188364-77-4, 188924-03-0, 189154-62-9, 191743-71-2, 201163-43-1, 206357-86-0, 221638-71-7, 225502-44-3, 270910-26-4, 307928-07-0, 356055-70-4, 391229-98-4
MF (C2 H4 O)n H2 O
CI PMS, COM
PCT Polyether
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DETHERM*, DIOGENES, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2, HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC, PDLCOM*, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, TULSA, ULIDAT, USAN, USPAT2, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

73703 REFERENCES IN FILE CA (1907 TO DATE)
18636 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
73826 REFERENCES IN FILE CAPLUS (1907 TO DATE)

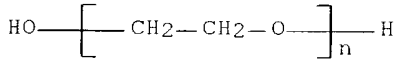
=> S POLYETHYLENE GLYCOL/CN
L3 1 POLYETHYLENE GLYCOL/CN

=> D

L3 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 25322-68-3 REGISTRY
CN Poly(oxy-1,2-ethanediyl), α-hydro-ω-hydroxy- (9CI) (CA INDEX

NAME)
OTHER NAMES:
CN α,ω-Hydroxypoly(ethylene oxide)
CN α-Hydro-ω-hydroxypoly(oxy-1,2-ethanediyl)
CN α-Hydro-ω-hydroxypoly(oxyethylene)
CN 1,2-Ethanediol, homopolymer
CN 1660O
CN 1660S
CN 400DAB8
CN Alkox
CN Alkox E 100
CN Alkox E 130
CN Alkox E 160
CN Alkox E 240
CN Alkox E 30
CN Alkox E 45
CN Alkox E 60
CN Alkox E 75
CN Alkox R 1000
CN Alkox R 15
CN Alkox R 150
CN Alkox R 400
CN Alkox SR
CN Antarox E 4000
CN Aquacide III
CN Aquaffin
CN Badimol
CN BDH 301
CN Bradsyn PEG
CN Breox 2000
CN Breox 20M
CN Breox 4000
CN Breox 550
CN Breox PEG 300
CN CAFO 154
CN Carbowax
CN Carbowax 100
CN Carbowax 1000
CN Carbowax 1350
CN Carbowax 14000
CN Carbowax 1450
CN Carbowax 1500
CN Carbowax 1540
CN Carbowax 20
CN Carbowax 200
CN Carbowax 20000
CN Carbowax 25000
CN Carbowax 300
CN Carbowax 3350
CN Carbowax 400
CN Carbowax 4000
CN Carbowax 4500
CN **Polyethylene glycol**
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY
AR 9002-90-8
DR 615575-04-7, 12676-74-3, 12770-93-3, 9081-95-2, 9085-02-3, 9085-03-4, 54510-95-1, 125223-68-9, 54847-64-2, 59763-40-5, 64441-68-5, 64640-28-4, 133573-31-6, 25104-58-9, 25609-81-8, 134919-43-0, 101677-86-5, 99264-61-6,

106186-24-7, 112895-21-3, 114323-93-2, 50809-04-6, 50809-59-1,
119219-06-6, 60894-12-4, 61840-14-0, 37361-15-2, 112384-37-9, 70926-57-7,
75285-02-8, 75285-03-9, 77986-38-0, 150872-82-5, 154394-38-4, 79964-26-4,
80341-53-3, 85399-22-0, 85945-29-5, 90597-70-9, 88077-80-9, 88747-22-2,
34802-42-1, 107502-63-6, 107529-96-4, 116549-90-7, 156948-19-5,
169046-53-1, 188364-77-4, 188924-03-0, 189154-62-9, 191743-71-2,
201163-43-1, 206357-86-0, 221638-71-7, 225502-44-3, 270910-26-4,
307928-07-0, 356055-70-4, 391229-98-4
MF (C2 H4 O)n H2 O
CI PMS, COM
PCT Polyether
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, AQUIRE, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CABA, CANCERLIT, CAPLUS, CASREACT, CBNB, CEN, CHEMCATS,
CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU, DETHERM*,
DIOGENES, DRUGU, EMBASE, ENCOMPLIT, ENCOMPLIT2, ENCOMPPAT, ENCOMPPAT2,
HSDB*, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, MSDS-OHS, NIOSHTIC,
PDLCOM*, PIRA, PROMT, RTECS*, SPECINFO, TOXCENTER, TULSA, ULIDAT, USAN,
USPAT2, USPATFULL, VETU, VTB
(*File contains numerically searchable property data)
Other Sources: DSL**, TSCA**, WHO
(**Enter CHEMLIST File for up-to-date regulatory information)



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

73703 REFERENCES IN FILE CA (1907 TO DATE)
18636 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
73826 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> S URICASE
L4 35 URICASE

=> S URICASE/CN
L5 1 URICASE/CN

=> D

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2004 ACS on STN
RN 9002-12-4 REGISTRY
CN Oxidase, urate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN E.C. 1.7.3.3
CN Urate oxidase
CN Urate: O2-oxidoreductase
CN Uratoxidase
CN Uric acid oxidase
CN **Uricase**
CN Uricozyme
MF Unspecified
CI MAN
LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS,
BIOSIS, BIOTECHNO, CA, CAPLUS, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM,
DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, IPA, MEDLINE, MRCK*, PHAR,

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        PROMT, RTECS*, TOXCENTER, USPAT2, USPATFULL
          (*File contains numerically searchable property data)
      Other Sources:   EINECS**, TSCA**
          (**Enter CHEMLIST File for up-to-date regulatory information)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
             1839 REFERENCES IN FILE CA (1907 TO DATE)
               77 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
             1842 REFERENCES IN FILE CAPLUS (1907 TO DATE)

FILE 'CAPLUS' ENTERED AT 15:06:32 ON 12 APR 2004

=> S L3 OR (POLYETHYLENE GLYCOL);S L5 OR URICASE
          74015 L3
         305423 POLYETHYLENE
          10652 POLYETHYLENES
         308630 POLYETHYLENE
                  (POLYETHYLENE OR POLYETHYLENES)
         310773 GLYCOL
          42002 GLYCOLS
         325152 GLYCOL
                  (GLYCOL OR GLYCOLS)
          86032 POLYETHYLENE GLYCOL
                  (POLYETHYLENE(W)GLYCOL)
L6       119962 L3 OR (POLYETHYLENE GLYCOL)


           1845 L5
           1958 URICASE
             28 URICASES
           1961 URICASE
                  (URICASE OR URICASES)
L7         2553 L5 OR URICASE

=> S POLYETHYLENEGLYCOL
           2611 POLYETHYLENEGLYCOL
             80 POLYETHYLENEGLYCOLS
L8         2663 POLYETHYLENEGLYCOL
                  (POLYETHYLENEGLYCOL OR POLYETHYLENEGLYCOLS)

=> S L6 OR L8
L9       121017 L6 OR L8

=> S 12000 OR 12;S 15000 OR 15;S 20000 OR 20;S 30000 OR 30
           1092 12000
        1252430 12
L10     1253393 12000 OR 12


           1271 15000
        1511556 15
L11     1512604 15000 OR 15


           1532 20000
        2070615 20
L12     2071810 20000 OR 20


            808 30000
```

```
       1680830 30
L13    1681499 30000 OR 30
 75% OF LIMIT FOR TOTAL ANSWERS REACHED

=> S (L10,L11,L12,L13) AND L9
L14      50330 ((L10 OR L11 OR L12 OR L13)) AND L9

=> S L14 AND L7
L15         21 L14 AND L7

=> S ENZYME
        701596 ENZYME
        404704 ENZYMES
L16     883822 ENZYME
                (ENZYME OR ENZYMES)
 95% OF LIMIT FOR TOTAL ANSWERS REACHED

=> S L14 AND L16
L17       1664 L14 AND L16

=> D L15 1-21 CBIB ABS

L15  ANSWER 1 OF 21  CAPLUS  COPYRIGHT 2004 ACS on STN
2002:762731   Document No. 138:260234  Uricase formulated with
     polyethylene glycol (uricase-PEG 20
     ): biochemical rationale and preclinical studies.  Bomalaski, John S.;
     Holtsberg, Frederick W.; Ensor, C. Mark; Clark, Mike A. (Department of
     Biology, University of Kentucky, Lexington, KY, USA).  Journal of
     Rheumatology, 29(9), 1942-1949 (English) 2002.  CODEN: JRHUA9.  ISSN:
     0315-162X.  Publisher: Journal of Rheumatology Publishing Co. Ltd..
AB   Humans have a non-sense codon inserted into the 5 prime end of the open
     reading frame of urate oxidase, and thus express an enzymically inactive
     fragment of this enzyme; and consequently are unable to metabolize uric acid
     into allantoin and are prone to develop hyperuricemia and gout. Various urate
     oxidases (uricase) from mammals and microorganisms were administered to humans
     with hyperuricemia and gout.  Although successful in lowering blood plasma
     uric acid, these therapies have had limited application due to undesirable
     biochem. properties of the enzymes used, the short circulating half-life, and
     inherent antigenicity of these prepns.  The authors compared urate oxidase
     from a variety of sources for specific enzyme activity, pH optimum, affinity,
     and retention of enzyme activity under physiol. conditions.  A variety of
     polyethylene glycols (PEG) were tested to formulate uricase.  Urate oxidase
     from Candida utilis had more favorable enzymic properties and PEG of 20,000 MW
     (termed uricase-PEG 20) had greatly reduced antigenicity and increased
     circulating half-life as compared to those previously described.  It is
     anticipated that uricase-PEG 20 may have utility as a treatment for
     hyperuricemia and gout.


L15  ANSWER 2 OF 21  CAPLUS  COPYRIGHT 2004 ACS on STN
2002:368277   Document No. 136:374515  Bleaching composition for keratinous
     fibers comprising an associative polyurethane.  Legrand, Frederic; De la
     Mettrie, Roland (L'oreal, Fr.).  PCT Int. Appl. WO 2002038117 A1 20020516,
     48 pp.  DESIGNATED STATES: W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR,
     BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB,
     GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,
     LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL,
     PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
     VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ,
     CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC,
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ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (French). CODEN: PIXXD2. APPLICATION: WO 2001-FR3429 20011106. PRIORITY: FR 2000-14320 20001108.

AB The invention concerns bleaching compns. for keratinous fibers, in particular human keratinous fibers and more particularly hair, comprising, in a medium suitable for bleaching, at least an oxidizing agent and furthermore at least a cationic associative polyurethane. The invention also concerns the bleaching method and devices using said composition A hair bleach contained 200 volume hydrogen peroxide **12**, stabilizer q.s., cationic polyurethane 0.3, pH adjusting agent q.s. pH = 4.7, and water q.s. 100 g. The composition is applied on the hair for 45 min , the hair is then rinsed with water.

L15 ANSWER 3 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN

2002:107165 Document No. 136:172754 Highly reactive branched polymer and proteins or peptides conjugated with the polymer. Park, Myung-Ok; Lee, Kang-Choon; Cho, Sung-hHe (S. Korea). PCT Int. Appl. WO 2002009766 A1 20020207, 47 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-KR1209 20010713. PRIORITY: KR 2000-44046 20000729.

AB The present invention relates to new biocompatible polymer derivs., and a protein-polymer or a peptide-polymer which is produced by conjugation of biol. active protein and peptide with the biocompatible polymer derivs. More particularly, the present invention relates to a highly reactive branched biocompatible polymer derivative containing a long linker between polymer derivs. and protein or peptide mols., which is minimized in decrease the biol. activity of proteins by conjugating the less number of polymer derivs. to the active sites of proteins, improved in water solubility, and protected from being degraded by protease. In hence, the highly reactive branched biocompatible polymer-proteins or peptides conjugates with long linker retain the biol. activity for a long period of time and improve a bioavailability of bioactive proteins and peptides. For example, activated PEG-interferon conjugates were prepared by adding 3 mg of succinic N-hydroxysuccinimidyl di-PEG to 3 mg of interferon in 0.1 M phosphate buffer solution, pH 7.0 at ambient temperature The reaction was stopped with 0.1 M glycine and the excess reagents were using Centricon-**30**.

L15 ANSWER 4 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN

2001:472447 Document No. 135:66017 Hair dye aerosol compositions containing water-soluble polymers. Noguchi, Mutsumi; Onuki, Takeshi; Mitamura, Joji (Lion Corporation, Japan). PCT Int. Appl. WO 2001045656 A1 20010628, 34 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (Japanese). CODEN: PIXXD2. APPLICATION: WO 2000-JP8987 20001219. PRIORITY: JP 1999-360313 19991220; JP 1999-360797 19991220.

AB Disclosed is a one-pack aerosol-type hair dye composition containing an oxidation dye and an oxidizing enzyme, characterized by further containing at least one water-soluble polymer selected from among hydroxypropyl cellulose,

CM-cellulose, xanthan gum, guar gum, locust bean gum, gum arabic, tragacanth gum, karaya gum, gellan gum, pectin, carrageenan, furcellaran, alginic acid and salts thereof, hyaluronic acid and salts thereof, chondroitin sulfate and salts thereof, ethylene oxide polymers, polyacrylic acid and salts thereof, acrylic acid copolymers and salts thereof, polyvinylpyrrolidone, vinylpyrrolidone copolymers, polyvinyl acetate, vinyl acetate copolymers and carboxyvinyl polymers. A hair dye aerosol composition containing p-phenylenediamine 1.5, p-aminophenol 0.1, methaphenylenediamine 0.**15**, hydroxypropyl cellulose (Niso HPC) 5, ethanol 5, lactic acid 0.5, oleic acid 0.1, sodium polyoxyethylene lauryl ether sulfate 0.2, laccase 0.3, monoethanol amine and water q.s. to 100 % was prepared

L15 ANSWER 5 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
2001:450870 Document No. 135:50857 Composition containing a mixture of two polyurethane polyethers for decoloring keratinic fibers. Legrand, Frederic (L'Oreal, Fr.). Eur. Pat. Appl. EP 1108418 A1 20010620, 23 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (French). CODEN: EPXXDW. APPLICATION: EP 2000-403211 20001117. PRIORITY: FR 1999-15678 19991213.
AB A composition for removing hair color is disclosed which comprises, in a milieu appropriate for decoloring, at least one oxidizing agent and at least one combination of two polyurethane polyethers. Said polyurethane polyether may be obtained by polycondensation of a **polyethyleneglycol**, stearyl alc., and methylene bis(4-cyclohexylisocyanate). Thus, a bleach comprises ceteareth **30** 2.2 g, Aculyn 44 0.1 g, Aculyn 46 0.2 g, stabilizers q.s., hydrogen peroxide up to **30** vols. 18 g, phosphoric acid q.s. to pH 2.5, distilled water q.s. to 100 g total.

L15 ANSWER 6 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
2001:384369 Document No. 136:79541 Diabetes insipidus in **uricase**-deficient mice: A model for evaluating therapy with poly(ethylene glycol)-modified **uricase**. Kelly, Susan J.; Delnomdedieu, Marielle; Oliverio, Michael I.; Williams, L. David; Saifer, Mark G. P.; Sherman, Merry R.; Coffman, Thomas M.; Johnson, G. Allan; Hershfield, Michael S. (Divisions of Rheumatology, Department of Medicine, Duke University School of Medicine, Durham, NC, USA). Journal of the American Society of Nephrology, 12(5), 1001-1009 (English) 2001. CODEN: JASNEU. ISSN: 1046-6673. Publisher: Lippincott Williams & Wilkins.
AB **Uricase**-deficient mice develop uric acid nephropathy, with high mortality rates before weaning. Urate excretion was quantitated and renal function was better defined in this study, to facilitate the use of these mice as a model for evaluating poly(ethylene glycol)-modified recombinant mammalian **uricases** (PEG-**uricase**) as a potential therapy for gout and uric acid nephropathy. The uric acid/creatinine ratio in the urine of **uricase**-deficient mice ranges from 10 to > **30**; on a weight basis, these mice excrete **20**- to 40-fold more urate than do human subjects. These mice consistently develop a severe defect in renal concentrating ability, resulting in an approx. sixfold greater urine volume and a fivefold greater fluid requirement, compared with normal mice. This nephrogenic diabetes insipidus leads to dehydration and death of nursing mice but, with adequate water replacement, high urine flow protects adults from progressive renal damage. Treatment of **uricase**-deficient mice with PEG-**uricase** markedly reduced urate levels and, when initiated before weaning, preserved the renal architecture (as evaluated by magnetic resonance microscopy) and prevented the loss of renal concentrating function. PEG-**uricase** was far more effective and less immunogenic than unmodified **uricase**. Retention of **uricase** in most mammals and its loss in humans and some other primates may reflect the evolution of renal function under different

environmental conditions. PEG-**uricase** could provide an effective therapy for uric acid nephropathy and refractory gout in human patients.

L15 ANSWER 7 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
2001:338762 Document No. 134:362292 Methods of determining individual hypersensitivity to a pharmaceutical agent from gene expression profile. Farr, Spencer (Phase-1 Molecular Toxicology, USA). PCT Int. Appl. WO 2001032928 A2 20010510, 222 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US30474 20001103. PRIORITY: US 1999-PV165398 19991105; US 2000-PV196571 20000411.

AB The invention discloses methods, gene databases, gene arrays, protein arrays, and devices that may be used to determine the hypersensitivity of individuals to a given agent, such as drug or other chemical, in order to prevent toxic side effects. In one embodiment, methods of identifying hypersensitivity in a subject by obtaining a gene expression profile of multiple genes associated with hypersensitivity of the subject suspected to be hypersensitive, and identifying in the gene expression profile of the subject a pattern of gene expression of the genes associated with hypersensitivity are disclosed. The gene expression profile of the subject may be compared with the gene expression profile of a normal individual and a hypersensitive individual. The gene expression profile of the subject that is obtained may comprise a profile of levels of mRNA or cDNA. The gene expression profile may be obtained by using an array of nucleic acid probes for the plurality of genes associated with hypersensitivity. The expression of the genes predetd. to be associated with hypersensitivity is directly related to prevention or repair of toxic damage at the tissue, organ or system level. Gene databases arrays and apparatus useful for identifying hypersensitivity in a subject are also disclosed.

L15 ANSWER 8 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
2000:117191 Document No. 132:148491 Urate oxidases of pig and baboon and the genes encoding them and the development of serum-stable non-immunogenic enzymes for the therapeutic breakdown of uric acid. Hershfield, Michael; Kelly, Susan J. (Duke University, USA). PCT Int. Appl. WO 2000008196 A2 20000217, 69 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US17678 19990805. PRIORITY: US 1998-95489 19980806.

AB **Uricases** that show sequence similarities to the **uricase** found at extremely low levels in the human liver are identified in pig and baboon and cDNAs encoding them are cloned for treatment of hyperuricemia and hyperuricosuria, e.g. gout and as a complication of leukemia. The proteins may be used to create novel **uricases**, such as fusion proteins, with low immunogenicity or improved serum stability and bioavailability. CDNAs were cloned from liver by standard RT-PCR methods and two fusion proteins with N-terminal regions from the pig enzyme and C-terminal regions from the baboon enzyme were constructed by

standard methods. The fusion proteins showed ≥5-fold higher specific activity than the baboon enzyme and ≥1.2-fold higher specific activity than the pig enzyme. The PEGylated form of one of the fusion proteins retained 62% of its activity with near normal kinetic properties. In mice, the PEGylated enzyme had a circulating half-life of about 48 h compared to <2 h for the unmodified enzyme.

L15 ANSWER 9 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
1999:337765 Document No. 131:134509 Biopharmaceutical Properties of **Uricase** Conjugated to Neutral and Amphiphilic Polymers. Caliceti, Paolo; Schiavon, Oddone; Veronese, Francesco M. (Department of Pharmaceutical Sciences, University of Padova, Padua, 35131, Italy). Bioconjugate Chemistry, 10(4), 638-646 (English) 1999. CODEN: BCCHES. ISSN: 1043-1802. Publisher: American Chemical Society.

AB A comparative pharmacokinetic and biodistribution investigation of polymer-protein conjugates prepared with various amphiphilic polymers was carried out using **uricase** as a model. Four polymer- **uricase** derivs. have been obtained by covalent binding of a similar number of polymer chains of (a) linear poly(ethylene glycol) (Mw 5000 Da); (b) branched **polyethylene glycol** (PEG) (Mw 10 000 Da); (c) poly(N-vinylpyrrolidone) (PVP) (Mw 6000 Da); (d) poly(N-acryloylmorpholine) (PAM) (Mw 6000 Da). By i.v. administration to Balb/c mice, the conjugates displayed different pharmacokinetic and organ distribution behaviors. (1) The unmodified enzyme and the PVP conjugate were the enzyme forms with the shortest and the longest permanence in blood resp. (mean residence time 45 and 4378 min). (2) Native **uricase** was found to localize soon after administration significantly in heart, lungs, and liver from where it was also rapidly cleared. (3) The PAM derivative showed the highest concentration levels in liver (up to 25.5% of the dose) and considerable accumulation took also place in the other considered organs. (4) PVP-**uricase** displayed a relevant tropism for liver but low uptake indexes were found for the other organs. (5) The branched PEG derivative accumulated preferentially in liver and spleen. (6) The linear PEG conjugate was, among the various **uricase** forms, the species with the lowest distribution levels in all the examined organs. (7) Finally, all the enzyme forms slowly disposed in kidneys with higher levels for the PAM derivative (**15**% after 2880 min) and unmodified **uricase** (14% after 1440 min).

L15 ANSWER 10 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
1999:162031 Document No. 131:15941 Crosslinking of chitosan membrane with **polyethylene glycol** diglycidyl ether for immobilization of **uricase**. Suye, Shin-ichiro; Mizusawa, Atsushi (Faculty of Engineering, Fukui University, Bunkyo, Fukui, 910-8507, Japan). Sen'i Gakkaishi, 55(2), 73-77 (English) 1999. CODEN: SENGA5. ISSN: 0037-9875. Publisher: Sen'i Gakkai.

AB This paper describes the immobilization of **uricase** by entrapment. The entrapping membrane was prepared by the crosslinking of chitosan with **polyethylene glycol** diglycidyl ether (diepoxy compound). The properties of the immobilized enzyme were investigated and compared with those of the native **uricase**. The enzyme activity of the immobilized **uricase** were found to be more dependent on temperature and pH than that of the native enzyme. The **uricase** immobilized membrane was sufficiently stable for **30** days allowing for the determination of uric acid concentration The uric acid sensor was constructed using a hydrogen peroxide electrode.

L15 ANSWER 11 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
1992:449257 Document No. 117:49257 Modification of peptides with **polyethyleneglycol** monomethyl ether mono(glyoxylylphenyl) ether.

Sano, Akihiko; Maeda, Hiroo; Kai, Hiroyuki; Ono, Keiichi (Sumitomo Pharmaceuticals Co., Ltd., Japan). Jpn. Kokai Tokkyo Koho JP 03148298 A2 19910625 Heisei, 12 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1989-285927 19891101.

AB Calcitonin-related peptides, e.g., elastase, atrial natriuretic factor, gonadotropins, α-melanotropin, parathyroid hormone, IGF-II, **uricase**, are modified with R(OCH2CH2)nOC6H4COCHO (I; n = integer such that the average mol. weight of the **polyethyleneglycol** is 1000- **12**,000; R = alkyl]. **Polyethyleneglycol** monomethyl ether (average mol. weight 5000) was esterified with p-toluenesulfonyl chloride to give the corresponding **polyethyleneglycol** monomethyl ether tosylate, which was condensed with 4-HOC6H4COCHO to give MeO(CH2CH2)nOC6H4COCHO, whose oxidation with SeO2 gave the corresponding p-I [R = Me; average mol. weight 5000] (II). To a solution of elastase containing NaHCO3 and Na2CO3 was added a 10% solution of 2-methylmaleic anhydride in acetone at room temperature, the resulting mixture, adjusted to pH 9-10 with 1N NaOH and then treated with II in the dark at room temperature for 18 h, HOAc added, and the resulting mixture warmed at 40° for 4 h to give an aqueous solution of the modified peptide.

L15 ANSWER 12 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN

1990:4065 Document No. 112:4065 Biosensor for lactate determination. Musil, Jan; Racek, Jaroslav (Czech.). Czech. CS 260913 B1 19890414, 5 pp. (Czech). CODEN: CZXXA9. APPLICATION: CS 1985-4194 19850611.

AB In a Clark-type biosensor for lactic acid determination, the surface of the Pt electrode is immersed in a hollow cavity (**20**-50 μL volume) covered with a semipermeable membrane. The cavity contains immobilized cells (immobilized in, e.g. agar) and optionally **uricase**. A suspension of Hansenula canomala (cultivated in the presence of lactate) was placed in a depression in the surface of a Pt electrode and covered with an acetyl cellulose membrane. Serum (0.3 mL) was diluted with 3 mL phosphate buffer (pH 7.2) containing K3Fe(CN)6. After 1 min at 25° the current was measured. A current of 0.55 μA corresponded to lactic acid 1 mM.

L15 ANSWER 13 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN

1988:469932 Document No. 109:69932 Biological fluid measuring device having replaceable membranes which cooperate with an enzyme electrode assembly. Shults, Mark C.; Capelli, Christopher C.; Updike, Stuart J. (Markwell Medical Institute, Inc., USA). PCT Int. Appl. WO 8706342 A1 19871022, 45 pp. DESIGNATED STATES: W: AU, DK, FI, JP, NO; RW: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1987-US822 19870410. PRIORITY: US 1986-852343 19860415; US 1986-852346 19860415.

AB This device, for determining the presence and amts. of substances in a biol. fluid without the need for dilution of the fluid, comprises a main housing including electronic circuit means and ≥1 electrode and a cartridge having a membrane. The cartridge is removably mounted on the housing and the membrane is operably associated with the electrode. The cartridge also includes means for protecting the membrane when the device is not in use. Polyurethanes were prepared by solution polymerization techniques as block copolymers which were tough and elastic and were solution cast in N,N-dimethylformamide to yield clear films that demonstrated good wet strength when swollen in H2O. In an enzyme electrode assembly to monitor glucose concns. in a fluid sample, the membrane layer nearest the anode (the inner layer) comprised a block copolymer (.apprx.0.5-3μ thick) permeable to H2O2 but which restricts the passage of higher mol. weight substances. The block copolymer membrane layer (**20**-35μ thick) nearest the sample (the outer layer) functioned as a diffusion barrier to prevent passage of high mol. weight substances and limited the amount of

glucose that passed through. An intermediate layer binding the inner and outer layers together included glucose oxidase combined with a block copolymer. For ease of application in the electrode assembly, an appropriate carrier or frame made of cardboard, rubber or plastic was secured to the surface of the laminate or multilayered membrane. The frame included an opening in the central portion where the outer layer of the membrane was exposed to the electrode.

L15 ANSWER 14 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
1986:2519 Document No. 104:2519 Dressing protein. Enzymes solubilized in organic solvent and their application as chemicals. Futami, Ayako; Inada, Yuji (Tokyo Inst. Technol., Tokyo, Japan). Kagaku (Kyoto, Japan), 40(10), 650-5 (Japanese) 1985. CODEN: KAKYAU. ISSN: 0451-1964.
AB A review with **20** refs., on the functions of lipase, chymotrypsin, and hemoproteins chemical modified with **polyethylene glycol** in organic solvents. The use of such proteins, as anticancer drugs and allergens, is also described; examples include asparaginase, **uricase**, neocarzinostatin, and albumin.

L15 ANSWER 15 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
1985:539940 Document No. 103:139940 Studies on antigenicity of the **polyethylene glycol** (PEG)-modified **uricase**.
Tsuji, Junichi; Hirose, Katsumi; Kasahara, Etsuko; Naitoh, Maki; Yamamoto, Itaru (Toyobo Res. Cent., Toyobo Co., Ltd., Ohtsu, 520-02, Japan). International Journal of Immunopharmacology, 7(5), 725-30 (English) 1985. CODEN: IJIMDS. ISSN: 0192-0561.
AB The purified **uricase** (urate: oxygen oxidoreductase, EC. 1.7.3.3) from Candida utiliz was modified to varying degrees with monomethoxypolyethylene glycol (PEG) of different mol. wts. using cyanuric chloride as the coupling reagent. The PEG-**uricase** conjugates were examined for their immunol. properties by means of ring test and passive cutaneous anaphylaxis (PCA). As increasing amts. of PEG were attached to **uricase**, it showed a decreasing ability to elicit antibody production in rabbits. When sufficient polymers were attached, the modified **uricase** was devoid of the capacity to combine in vivo and in vitro with antibodies from guinea pigs injected with the unmodified **uricase**; however, it was still able to react with antibodies to PEG-**uricase** conjugate. Antibodies against PEG-**uricase** conjugates also reacted with PEG modified superoxide dismutase (superoxide: superoxide oxidoreductase, EC 1.**15**.1.1). Thus, the coupling of PEG to **uricase** resulted in the loss of the original antigenicity and immunogenicity, but also in the appearance of new antigenicity and immunogenicity which did not show any cross-reaction with the native **uricase**.

L15 ANSWER 16 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
1982:223276 Document No. 96:223276 Sustained-release enzyme formulations. (Japan Atomic Energy Research Institute, Japan). Jpn. Kokai Tokkyo Koho JP 57032213 A2 19820220 Showa, 4 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1980-108031 19800806.
AB Sustained-release therapeutic enzyme prepns. are prepared by mixing the enzyme with vinyl polymerizable monomers and polymerizing the mixture with ionizing radiation or light. Thus, **uricase** [**9002-12-4**] 0.01, pH 8.5 borate buffer 1.**15**, **polyethylene glycol** dimethacrylate 0.6, and trimethylolpropane trimethacrylate 0.25 g were mixed and irradiated by γ-rays at 5 + 105 rads for 2 h at -78°. The release of **uricase** from this formulation into saline at 37° was 0.08, 0.28, and 0.51 mg at 10, **30**, and 60 days, resp.

L15 ANSWER 17 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
1981:583503 Document No. 95:183503 Enzyme and reagent-impregnated paper for electrical tests. (Sonoda, Masaru, Japan). Jpn. Kokai Tokkyo Koho JP 56097235 19810805 Showa, 4 pp. (Japanese). CODEN: JKXXAF. APPLICATION: JP 1979-172755 19791228.

AB A body fluid sample was applied to a piece of paper which had been impregnated with enzymes and color reagents, and the intensity or change of color of the paper was correlated with the concentration of the body fluid components. Thus, a paper disk (diameter 5 mm, thickness 1 mm) was treated with 0.5% periodic acid for **30** min, washed, and dried. The disk was impregnated with 0.1M phosphate buffer (pH 7.2) containing cholesterol esterase, cholesterol oxidase, peroxidase, **polyethylene glycol**, 4-aminoantipyrine, and phenol. When blood serum (**20** μL) was applied to the disk, the color changed depending upon the concentration of cholesterol in the serum. Normal serum produced maroon, whereas serum with 100 and 250 mg cholesterol/dL produced pink and orange colors, resp.

L15 ANSWER 18 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
1979:553575 Document No. 91:153575 Modification of yeast **uricase** with **polyethylene glycol**: disappearance of binding ability towards anti-**uricase** serum. Nishimura, Hiroyuki; Ashihara, Yoshihiro; Matsushima, Ayako; Inada, Yuji (Lab. Biol. Chem., Tokyo Inst. Technol., Tokyo, 152, Japan). Enzyme, 24(4), 261-4 (English) 1979. CODEN: ENZYBT. ISSN: 0013-9432.

AB **Uricase** from Candida utilis was modified with activated **polyethylene glycol** (2-O-methyoxypolyethylene glycol-4,6-dichloro-s-triazine) of 5000 daltons mol. weight The modification of 43% of the total amino groups in the **uricase** mol. gave rise to a complete loss of the binding ability towards antiuricase serum from rabbits. This modified **uricase** retained **15**% of the enzymic activity of non-modified **uricase**.

L15 ANSWER 19 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
1979:416275 Document No. 91:16275 Enzymic determination of uric acid. Bretaudiere, Jean Pierre; Hung Thieu Phung (Fr.). Fr. Demande FR 2383443 19781006, 6 pp. (French). CODEN: FRXXBL. APPLICATION: FR 1977-6656 19770307.

AB Methods and reagents are described for the enzymic determination of uric acid (I) in body fluids by use of **uricase** (II) isolated from Aspergillus flavus, horseradish peroxidase (III), and a chromogenic H donor comprised of 2 compds., either PhOH and aminophenazone (IV) or 3-hydroxybenzoic acid (V) (or a salt) and IV. A stable colored derivative is formed that can be quantitated photometrically or spectrometrically. The reagents, which may be in tablet form or in aqueous or aqueous-organic solns., are comprised of the following: a buffer to maintain pH at 6.8-8.7; 1-300 IU/mL (at 25°) of II from A. flavus; 1000-150,000 units III/L; 0.1-10 g IV/L; 0.2- **20** g PhOH or V/L; 0.1-10 mg of Na or K salt of EDTA/L; and 0.5-10 g **polyethylene glycol** (2000, 4000, or 6000)/L. For preparation of tablets, lactose, mannitol, polyvinylpyrrolidone, or sorbitol is combined with the reagents, and to eliminate interference by natural H donors or drugs, the sample containing I is preincubated in a solution of 0.001-10 mM final concentration of a Cu2+ or Fe3+ salt. The method is rapid, may be performed manually or automatically, and detns. may be made with either equilibrium or kinetic operating modes.

L15 ANSWER 20 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN
1978:559776 Document No. 89:159776 Product for clarifying serums. (Boehringer Mannheim G.m.b.H., Fed. Rep. Ger.). Belg. BE 858883 19780320, 14 pp. (French). CODEN: BEXXAL. APPLICATION: BE 1977-181060 19770920.

AB A reagent for clarifying turbid serum samples for photometric anal. in clin. chemical is described. The reagent consists of ≥1 mono- or di-esters of **polyethylene glycol** and of C9-C14 fatty acids containing a maximum of 8 ethylene oxide fragments, and solubility-improving agents, with the ester or group of esters presenting a hydrophilic-lipophilic balance of 8-**12**.8. The reagent consists primarily of lauric acid esters and contains polyglycol esters (3-4 ethylene oxide fragments/fatty acid radical) at 10-40% in weight The agents used for improving solubility are lower alkanols (C1-C3), glycols (up to C7), or polyglycol (up to 8 ethylene oxide fragments), and(or) surface-active agents. The surface-active agents are ethers of **polyethylene glycol** and C8-C16 alkanols containing 8-14 ethylene oxide fragments. The reagent is free of acid and aldehyde. Thus, H3BO3 and **polyethylene glycol** are mixed, heated for 2 h at 90° under vacuum, and held at this temperature for 6 h. The solution is cooled, and then lauric acid and p-toluenesulfonic acid are added. The mixture is heated for 2 h at 100° and held at this temperature for an addnl. 2 h. The solution is hydrolyzed by mixing with water for 1 h. The solution is then saturated with NaCl and extracted 3 times with EtOAc. The ester phases are dried, concentrated to .apprx.100 mL, mixed with basic alumina, and free fatty acids are eliminated by thin-layer chromatog. The solution is filtered and the solvent eliminated under vacuum. To determine uric acid in serum, a turbid serum sample is mixed with a solution containing K4P2O4, NAD, catalase, alkaline dehydrogenase, EtOH, and clarifying reagent. After 5 min at room temperature, the sample is clarified. **Uricase** is then added, and the absorbance is monitored at 334 nm.

L15 ANSWER 21 OF 21 CAPLUS COPYRIGHT 2004 ACS on STN

1976:146935 Document No. 84:146935 Protected polypeptide, essentially nonimmunogenic, enzymically active substance, and method for the extensive suppression of the immunogenicity of a polypeptide. Davis, Frank F.; Van Es, Theodorus; Palczuk, Nicholas C. (Research Corp., USA). Ger. Offen. DE 2433883 19760205, 33 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1974-2433883 19740715.

AB Enzymes and insulin were bound to **polyethylene glycol** derivs. yielding modified polypeptides which were enzymically active but did not give immunol. reactions in vivo or in vitro. **Uricase**, catalase, cholesterol **20**-hydroxylase, UDP-glycuronyltransferase, lysozyme, trypsin, and aldolase were modified by coupling to **polyethylene glycol** derivs. such as **polyethylene glycol**-4-hydroxy-6-chloro-1,3,5-triazine, **polyethylene glycol**-carboxymethylazide, **polyethylene glycol** -succinate, and **polyethylene glycol** amide. These polypeptide derivs. have potential uses in medicine since they are nonimmunogenic.